US Army Medical Research and Materiel

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Method of Measuring Tumor Suppressor Gene p53

Features and advantages:

- **Quantifies expression of the tumor suppressor gene p53**
- **Uses a plasmid to generate the RNA comparison standard**
- **RNA molar concentration is measured by spectrophotometry**

This invention provides a means for quantifying the level of activity of an important tumor suppressor gene, p53, by measuring the messenger ribonucleic acid (mRNA) level expressed by p53 and comparing it to a standard. A reverse transcriptase polymerase chain reaction (RT-PCR) assay is used to measure p53 mRNA. The RNA standard is generated by a plasmid which is part of the invention. The PCR-generated signal from human peripheral mononuclear blood cells (PMBC) is compared to the PCR-generated signal from serial dilutions of the standard.

During normal cell growth, it is believed growth-promoting proto-oncogenes are counterbalanced by growth-constraining tumor suppressor genes. Mutations and diseases such as HIV may contribute to an imbalance in the expression of these genes. The p53 gene is expressed in most normal tissues and mutations to it occur frequently in human malignancies. Thus, a method for measuring p53 levels may provide a useful indication of cancer and other diseases. PMBCs were obtained from HIV positive patients and negative controls and used in the assay. An incidental spike in p53 RNA and apoptosis on day 4 followed by a 20-fold increase in p24 antigen from day 0 to day 8 suggest an order of events in HIV infection, presumably with the increase in p53 occurring followed closely by apoptosis and then the production of virus from those remaining CD4+ T-cells that were spared. The data revealed an inverse association between p53 expression and HIV disease progression when two widely accepted parameters, CD4+ T-cell number and serum viral burden, were used. The invention can provide a means for disease monitoring and progression prediction.

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